UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/769,218	01/30/2004	Yigong Shi	112911.151	9564

7590 08/21/2007

Pepper Hamilton LLP
Firm 21269
One Mellon Center, 50th Floor
500 Grant Street
Pittsburgh, PA 15219

EXAMINER	
KIM, ALEXANDER D	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
08/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/769,218	SHI, YIGONG	
	Examiner	Art Unit	
	Alexander D. Kim	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 26-62* is/are pending in the application.

4a) Of the above claim(s) *1-19,26-52 and 56-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-23 and 53-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/13/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office actions, a non-Final rejection (mailed on 10/23/2006), Applicants filed a response and amendment received on 04/20/2007. Said amendment cancelled Claims 24-25, amended Claims 20-23 and added new Claims 53-62. Thus, Claims 1-23, 26-62 are pending in the instant office action.

Newly submitted claim 56-62 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The newly filed claims 56-62 are drawn to a method for identifying an inhibitor of an initiator caspase comprising new method steps, whereas previous examined claims are drawn to a method of inhibiting activity of a caspase-9.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 56-62 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

The claims 1-19 and 26-52 are withdrawn as being drawn to a non elected invention. Thus, Claims 20-23 and 53-55 will be examined herein.

Priority

2. Applicants argue the provisional application 60/443590 have support for the instant application. Reconsideration is requested.

In view of correction to the instant specification as well as filing of new Application Data Sheet (ADS), Examiner acknowledges the 60/443590 provides support for the instant application.

Information Disclosure Statement

3. The information disclosure statement (IDS) filed on 04/13/2007 with an appropriate fee has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Withdrawn-Objections to the Specification

4. The previous objection to the specification because the title is not descriptive of the claims is withdrawn by virtue of Applicant's amendment.

5. The previous objection to the Abstract for not completely describing the disclosed subject matter is withdrawn by virtue of Applicant's amendment.

6. The previous objection to the specification for instant application disclosing wrong provisional application 60/443,950 is withdrawn by virtue of Applicant's amendment.

7. The previous objection to the specification for reciting "the catalytic subunit of caspase-9 (residues 139-416, in vector pET-21b)" (see p. 33 line 14) is withdrawn by virtue of Applicant's amendment.

8. The previous objection to the specification reciting "BIR3 domain of XIAP (residues 252-350, in vector pBB75)" (see p. 33 line 15) is withdrawn by virtue of Applicant's amendment.

Claim Objections

9. Claim 54 is objected to because of the following informalities: Claim 54 recites "at amino". It is unclear if the claims are limited to the amino parts of the molecule of said amino acid residues. Appropriate correction is required.

Withdrawn-Claim Rejections - 35 USC § 112

10. The previous rejection of Claim 20-25 under 35 U.S.C. 112, second paragraph, is withdrawn by virtue of Applicant's amendment.

11. The previous rejection of Claim 20-25 under 35 U.S.C. 112, second paragraph, for having parentheses with SEQ ID NO, is withdrawn by virtue of Applicant's amendment.

12. The previous rejection of Claim 24 under of 35 U.S.C. 112, second paragraph, is withdrawn by virtue of canceling Claim 24

New-Claim Rejections - 35 USC § 112

13. Claims 20-23 and 54 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 recites the limitation of positions "Pro325", "Gly326", "His343" and "Leu344", which are a relative term. The position number used in the claim to describe specific amino acid residues of XIAP BIR3 is unclear without the point of reference, preferably identified by SEQ ID No. Appropriate clarification is required.
The instant rejection is necessitated by the amendment.

Claim 54 recites the limitation of positions "Leu244", "Pro237", "Phe404" and "Phe406", which are a relative term. The position number used in the claim to describe specific amino acid residues of XIAP BIR3 is unclear without the point of reference, preferably identified by SEQ ID No. Appropriate clarification is required.

The instant rejection is necessitated by the amendment.

Maintained-Claim Rejections - 35 USC § 112

14. Claims 20-23 and 53-55 stand rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous Claims 20-25. In response to this rejection, applicants have amended Claims 20-23; cancelled Claims 24-25; and added new Claims 53-55; and traverse the rejection as it applies to the newly amended claims. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue the instant application provide specific examples and detailed description of protein-protein interface between an exemplary inhibitor and initiator caspase in paragraph 0031 to 0038. Applicants argue the claimed method is fully supported by the specification and would not require undue experimentation.

However, the instant claims are drawn to a method of inhibiting the activity any initiator caspase comprising: identifying any compound or any molecules having structure and function of residues Pro325, Gly326, His343 and Lue 344, combining said compound with any composition as long as it contains any initiator caspase. Claim 53 recites the limitation "the initiator caspase is caspase-9", wherein the caspase-9 encompasses any caspase-9 from any source, which would not be described by the instant specification or the prior art to put one of skill in possession of the claimed

caspase-9. A method of instant specification and prior arts do not describe a method of inhibiting any initiator caspase, any caspas9 from any source by any compound, wherein any caspase or compound have unlimited structural limitation as long as it

The instant specification teaches a method for inhibiting a protease activity of human caspase-9 by forming 1:1 complex with the polypeptide of SEQ ID NO: 2 which is a human BIR3 domain comprising P325, G326, H343 and L344 or method of inhibiting a effector caspase (procaspase-3) activity in the mixture containing inactivated mammalian caspase-9 complex with the polypeptide of SEQ ID NO: 2 which is a BIR3 domain comprising P325, G326, H343 and L344. However, the breadth of claim includes those methods of inhibiting the activity any initiator caspase comprising: identifying any compound or any molecules having structure and function of residues Pro325, Gly326, His343 and Lue 344, combining said compound with any composition as long as it contains any initiator caspase. The prior art and instant specification teach a method of inhibiting human caspase-9 catalytic activity by forming complex with a polypeptide containing BIR domain thus inhibiting human procaspase-3 activity by blocking process of procaspase-3 (Deveraux et al. 1999, The EMBO Journal, Vol. 18 p. 5242-5251). The examples of methods described by prior art and instant specification do not describe a method of using any other inhibitor molecule(s) encompassed by the scope of the claims for inhibiting any initiator caspase with any molecule having any structure and function of Pro325, gly326, His343 and Leu344 of XIAP BIR3; sufficiently to represent the correlation between the structure and function of claimed genus method described above. Thus, the instant specification and the prior art cannot

describe the structure of a very broad claimed genus and one skilled in the art would not be in possession of the full scope of claimed methods.

15. Claims 20-23 and 53-55 stand rejected under 35 U.S.C. § 112; first paragraph, scope of enablement, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous Claims 20-25. In response to this rejection, applicants have amended Claims 20-23; cancelled Claims 24-25; and added new Claims 53-55; and traverse the rejection as it applies to the newly amended claims. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue the instant application provide specific examples and detailed description of protein-protein interface between an exemplary inhibitor and initiator caspase in paragraph 0031 to 0038. Applicants argue the claimed method is fully supported by the specification and would not require undue experimentation.

The nature of the invention is drawn to a method for inhibiting a protease activity of human caspase-9 by forming 1:1 complex with the human BIR3 domain which contains said four amino acid residues thus inhibiting a procaspase-3 activation by the inactivated capspase-9 and BIR3 complex. However, the breadth of claim includes a method of inhibiting the activity any initiator caspase comprising: identifying any

compound or any molecules having structure and function of residues Pro325, Gly326, His343 and Lue 344, combining said compound with any composition as long as it contains any initiator caspase. Applicants and the prior art teach one method of inhibiting protease activity of human caspase-9 thus inhibiting procaspase-3 activation with a peptide containing a human BIR3 domain with procaspase-3 as substrate as described in Example 3, p. 35 or Figure 5 of Deveraux et al. The instant specification disclose no direction or guidance on how to inhibit any initiator caspase or any caspase-9 from any source with any molecule having any structure and any function of Pro325, Gly326, His343 and Leu344 of XIAP BIR3. Thus the specification and prior art fail to describe how to make and use the claimed comprising genus molecules for inhibiting a genus initiator caspase sufficiently in claimed methods. Therefore, it is unpredictable for a claimed genus method as described above, wherein the unpredictable makes the level of skill required for one skill in the art very high. For all of the above reason, it would require undue experimentation necessary for a method of using the claimed genus of polypeptides.

Withdrawn-Claim Rejections - 35 USC § 101

16. The previous rejection of Claims 20-25 under 35 U.S.C. §101 is withdrawn by virtue of Applicant's amendment.

Maintained-Claim Rejections - 35 USC § 102

17. The previous rejection of Claims 20-23 and 53-55 under 35 U.S.C. 102(b) as being anticipated by Deveraux et al. (1999, The EMBO Journal, Vol. 18, p. 5242-5251) and Shiozaki et al. (2003, Molecular Cell, vol. 11, p. 519-527) is maintained. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

Claims 20-23 are drawn to a method of inhibiting activity of an initiator caspase comprising: identifying a compound having structure and function of amino acid Pro325, Gly326, His343 and Leu344 of XIAP BIR3; combining the compound with said initiator caspase and inhibiting the activity of the initiator caspase.

Applicant argues the Deveraux et al. fails to teach, suggest, or otherwise disclose a method for inhibiting an initiator caspase including the step of identifying a compound. However, as noted in the previous office action, Deveraux et al (1999) teach a method comprising testing the "ability to inhibit purified recombinant active caspases" and disclose a "BIR3-Ring" "inhibit active recombinant caspase-9" (emphasis added, see bottom of left column, p. 5247). The BIR3-Ring is encompassed by the recited compound in Claim 20; thus, teaching the step of identifying a compound.

Applicant notes that Deveraux states "experiments involving either BIR3 or Ring domain alone suggest that neither of these is sufficient to suppress caspases by itself" (page 5249, column 1, lines 9-11); thus, applicant argues the claim 20 describes critical amino acid for inhibition of caspase only in the BIR3 domain XIAP, which requires a Ring domain. However, as it is written, claim 20 encompasses any compound or molecule having structure and function of recited BIR3 domain residues. A compound

encompasse by claim 20 includes any molecule as long as it has any structure or function for inhibiting any caspase; thus, having or not having a Ring domain is irrelevant.

Applicant argue the Shiozaki et al is not a prior art. However, it is noted the "evidentiary reference" can be after the application's effective filing date or priority date. Applicant also argue the Shiozaki et al. is applicant's own work. However, Shiozaki et al. is considered as "by others" since the inventor and the authors of Shiozaki et al. are different.

As previously disclosed, the "BIR3 domain of Deveraux et al. (1999) would form 1:1 complex with caspase-9, wherein the BIR3-Ring contains sequence 243-497; thus meets all limitation of Claims 53-55. For the reasons above, the instant rejection is maintained.

Summary of Pending Issues

18. The following is a summary of the issues pending in the instant application:

a) Claim 54 is objected for reciting "at amino".

b) Claims 20-23 and 54 are rejected under of 35 U.S.C. 112, second paragraph.

c) Claims 20-23 and 53-55 are stand rejected under 35 U.S.C. § 112, first paragraph, written description.

d) Claims 20-23 and 53-55 are stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement.

e) Claims 20-23 and 53-55 stand rejected under 35 U.S.C. 102(b) as being anticipated by Deveraux et al. and Shiozaki et al.

Conclusion

19. Claims 20-23 and 53-55 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered section in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander D. Kim whose telephone number is (571) 272-5266. The examiner can normally be reached on 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alexander Kim

August 9, 2007

RICHARD HUTSON, PH.D.
PRIMARY EXAMINER